

**REMARKS**

Claims 3-6, 8, 9, and 20-30 are currently pending in this application. Claims 26-30 have been deemed withdrawn as drawn to non-elected species of opioid analgesic. As Applicants contend that claims directed to the elected species are free of the prior art and are otherwise allowable, Applicants respectfully request the Examiner broaden the search to include the species of Claims 26-30

Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Reconsideration and withdrawal of the rejections of this application in view of the remarks made herewith, is respectfully requested.

Applicants respectfully thank the Examiner for the withdrawal of the Obviousness rejections over Smith and Inturrisi.

**Rejections under 35 U.S.C. §103 (a)**

Claims 3-6, 8-9 and 20-25 are newly rejected under 35 U.S.C. §103(a) as being obvious over Dahlstrom et al *Journal of Pharmacokinetics and Biopharmaceutics*; 6(1), 1978, 41-43 ("Dahlstrom") in view of United States Patent No. 6,008,258 to Inturrisi ("Inturrisi"). Applicant respectfully traverses the rejection.

Dahlstrom describes a computer modeling of morphine and concludes that morphine produces analgesia a dose-dependent manner. Dahlstrom does not teach the combination of morphine with a second opioid analgesic, let alone any other drug.

As previously described, Inturrisi is related to treating tolerance and physical dependence in a subject having a NMDA receptor using d-methadone. Inturrisi states that the l-isomer of methadone is 50-fold more potent for the analgesic effect of the drug. In connection with this statement, Inturrisi cites a well-known publication, Olsen, G. D., et al. "Clinical Effects and Pharmacokinetics of Racemic Methadone and its Optional Isomers," *Clin. Pharmacol. Ther.*, 21:147-157 (1976). That is to say, the teachings of Inturrisi were well established within the art.

Nevertheless, the fact that l-methadone provides a greater analgesic response in humans does nothing to rectify the deficiencies of Dahlstrom in light of the general knowledge of the art.

The Examiner cites *In re Kerkhoven*, 625 F.2d 846 (CCPA 1980) for the proposition that it would be obvious to combine individual compositions taught to have the same utility to form a new composition for the same purpose. Applicant respectfully asserts that *In re Kerkhoven* does not apply to the treatment of pain. Indeed, Applicant previously argued that, prior to the present invention, the common strategy of one of ordinary skill in the art of combination therapy was to utilize two or more drugs of different mechanisms so as to reduce potential side effects.

To that end, Applicant submits herewith the Declaration of Dr. Charles E. Inturrisi, in which Dr. Inturrisi states that “at the time of the Application, one of ordinary skill in the art would not have been motivated to use a combination of two opioid analgesic agents to effect analgesia.” (Paragraph 8) Dr. Inturrisi explains that “prior to the Application, it was believed that use of two opioid analgesic agents would have had little added benefit as the two agents would compete for the same receptors and would thus be no more effective than using one agent at full dosage” (Paragraph 9). Indeed, the Smith paper (previously cited by the Examiner) shows this to be the case, as the combination of methadone and morphine in Smith did not result in even an additive effect from the combination; but, in fact, had a less desirable effect than using morphine alone.

Dr. Inturrisi describes that “if a second agent were to be used, *one of ordinary skill in the art at the time would have utilized an analgesic agent which acted on a different set of receptors*” (Paragraph 9, emphasis added). Dr. Inturrisi further states that he and his colleagues “would teach [their] pharmacology students that, in order to optimize the management of pain, they *should utilize a single opioid at a time...*” (Paragraph 10, emphasis added).

Thus, Applicant contends that one of ordinary skill in the art would have had no motivation to combine methadone with morphine, or any other opioid analgesic without potentially reducing the efficacy of both drugs. Furthermore, Applicants contend that one of ordinary skill in the art would have had no reasonable expectation of success in combining methadone and morphine as the two drugs are both opioid analgesics.

As such, Applicant respectfully submits that rejection under 35 U.S.C. §103(a) should be withdrawn.

### **CONCLUSION**

In view of the remarks made herein, Applicant submits that the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. If a telephone conference with Applicant's representative would be helpful in expediting prosecution of the application, Applicant invites the Examiner to contact the undersigned at the telephone number indicated below.

Applicant believes that no additional fees, other than the fee for the three-month extension of time, are required in connection with this paper. Nevertheless, Applicant authorizes the Director to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 04-1105, under Order No. 62076(51590).

Dated: January 14, 2010

Respectfully submitted,

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